Jarid2/Jumonji coordinates control of PRC2 enzymatic activity and target gene occupancy in pluripotent cells.

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Authors: Jamy C Peng, Anton Valouev, Tomek Swigut, Junmei Zhang, Yingming Zhao, Arend Sidow, Joanna Wysocka

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Public Summary:
Polycomb Repressive Complex 2 (PRC2) regulates key developmental genes in embryonic stem (ES) cells and during development. Here we show that Jarid2/Jumonji, a protein enriched in pluripotent cells and a founding member of the Jumonji C (JmjC) domain protein family, is a PRC2 subunit in ES cells. Genome-wide ChIP-seq analyses of Jarid2, Ezh2, and Suz12 binding reveal that Jarid2 and PRC2 occupy the same genomic regions. We further show that Jarid2 promotes PRC2 recruitment to the target genes while inhibiting PRC2 histone methyltransferase activity, suggesting that it acts as a "molecular rheostat" that finely calibrates PRC2 functions at developmental genes. Using Xenopus laevis as a model we demonstrate that Jarid2 knockdown impairs the induction of gastrulation genes in blastula embryos and results in failure of differentiation. Our findings illuminate a mechanism of histone methylation regulation in pluripotent cells and during early cell-fate transitions.

Scientific Abstract:
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